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(54) Title: TELLURIUM CONTAINING PRODUCT

(57) Abstract: A novel nutrient formulation containing tellurium for use in animals raised for meat production, and a method of feeding said nutrient formulation which improves subsequent livability, cumulative feed efficiency or weight gain is disclosed.



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BACKGROUND OF THE INVENTION:**Field of the Invention**

5 This invention relates to a tellurium containing nutritional formulation that enhances the cumulative weight gain and feed efficiency in animals raised for meat production and especially poultry. There is compelling evidence from the investigation of chick models that tellurium compounds act to influence the growth performance of chicks. The most cost effective use of tellurium compounds is at concentrations of 0.3-1.0 g/metric ton of feed.

Description of the Related Art

10 The present invention is based on the discovery that the addition of a tellurium species to the diet of poultry from the day of hatching increases the growth rate of the young chicks.

15 Prior research has shown that improvement of the quality of the nutrition of broilers have provided the possibility of increasing their growth rate in modern broiler strains. The increased growth is reflected in either an increased weight of the adult chicken, or a reduction in the period of time required for obtaining an adult chicken. According to the state of the art, at 14 days, approximately 50% of the broilers have a body weight of between 365 and 390 grams, and at 42 days, approximately 60% of the broilers have a body weight between 2100 and 2300 grams.

20 Growth of the young chick only starts after the yolk sac has been resorbed. Further, it is state of the art to deprive the hatched chick of nutrition in the first days of its life in order to enable it to exhibit compensatory growth. An earlier start of growth is reflected in an increased weight of the grown up chicken. It is, therefore, desirable to feed chicks a food composition that accelerates absorption of the yolk sac.

25 Materials promoting growth, the so-called "growth stimulants", are typically employed in animal feed for producing quicker growth and increased meat tissue production. The known growth promoting materials may be categorized as either antibiotics, synthetic chemical growth promoters, or sexual hormones. The use of sexual hormones has been forbidden in certain countries.

30 There are a number of prior art food compositions to enhance growth of young chicks. U.S. 6,258,399 discloses a composition containing monosaccharides, disaccharides and oligosaccharides fed immediately after hatching and during the first days of life that has a growth enhancing and mortality reducing effect.

Others have added various nutrients and vitamins to feed to prevent disease. For

example, U.S. 5,516,525 discloses the addition of vitamin D derivatives to animal feed to prevent development of tibial dyschondroplasia.

Increasing interest has been drawn to the substances known as trace elements, i.e. elements absolutely vital to the human organisms, albeit in minute amounts. Selenium is an essential trace element for proper physiological functioning in humans. Deficiency can lead to improper functioning of the body's metabolic processes, and to various diseases and disorders. Selenium deficiencies have been seen in people who rely on total parenteral nutrition (TPN) as their sole source of nutrition. Selenium deficiency is most commonly seen in China, where the selenium content in the soil, and therefore, selenium intake, is very low. It is characterized by Keshan Disease which results in an enlarged heart.

A blood selenium concentration of 0.02 g/ ml may be considered the critical threshold in defining a selenium deficiency. The Food and Drug Administration (FDA) established Recommended Dietary Allowance (RDA) for selenium at 55 g for adults and 70 g for lactating women.

Several studies reporting the beneficial effects of selenium supplementation in animals have appeared in the literature. In supplementation with intraruminal pellets of selenium the live weights of ewes receiving selenium were generally but not consistently higher than those of unsupplemented ewes. However, fleece weights were significantly greater in selenium supplemented ewes (Langerlands, J.P. et al; Subclinical Selenium Deficiency. 1-Selenium Status and the Response in Live Weight Gains and Wool Production of Grazing Ewes Supplemented With Selenium. 31 AUST. J. EXP. AGR. 25-31 (1991)). Supplementation with selenium has been observed to help lamb survival rates (Langerlands, J.P. et al; Subclinical Selenium Deficiency. 2- The Response in Reproductive Performance of Grazing Ewes Supplemented With Selenium. 31 AUST. J. EXP. AGR. 33-35 (1991)). Lamb weights increased significantly at all ages when their dams were supplemented with selenium (Langlands, J.P. et al; Subclinical Selenium Deficiency. 3- The Selenium Status and Productivity of Lambs Born to Ewes Supplemented With Selenium. 31 AUST. J. EXP. AGR. 37-43 (1990); Langlands, P.J. et al; Selenium Supplements for Grazing Sheep. 28 ANIMAL FEED SCI. TECH. 1-13 (1990)). Administration of selenium intraruminal pellets to dairy heifers resulted in weight gains of 0.11-0.12 kg/day over the control group (Wichtel, J.J. et al; The Effect of Intra-ruminal Se Pellets on Growth Rate, Lactation and Reproductive Efficacy in Dairy Cattle, 42 NEW ZEALAND VET. J. 205-210 (1994)).

Selenium has been recognized as an essential nutrient in the production of livestock because of its preventive action against certain diseases such as liver necrosis in pigs, white muscle disease in calves and lambs, and pancreatic degeneration and exudative diathesis

involving the capillaries in poultry. The level of selenium in feeds such as cereal grains and soybeans is in most areas inadequate to meet the nutritional needs of livestock. U.S. 4,042,722 discloses selenium containing additives for use as supplements in livestock feeds having a selenium content of not more than 5,000 ppm. Further, FDA has approved the use of selenium as a livestock feed supplement at levels of 0.1–0.3 ppm. Commercial trace mineral premixtures which are sometimes added to animal feed may contain MnO_2 , ZnO , FeSO_4 , FeCO_3 , CuSO_4 . Additionally, they sometimes contain trace amounts of selenium but not tellurium.

The nontoxic tellurium compound AS101, ammonium trichloro(dioxyethylene-O,O')tellurate, first developed by the present inventors has been shown to have beneficial effects in diverse preclinical and clinical studies. Most of its activities have been attributed in part to stimulation of endogenous production of a variety of cytokines. The immunomodulating properties of AS101 play a crucial role in preclinical studies demonstrating a protective effect in parasite and viral infected mice models, in autoimmune diseases, and in a variety of tumor models. AS101 has also been shown to have protective properties against lethal and sublethal effects of irradiation and chemotherapy, including protection from hemopoietic damage and alopecia, resulting in increased survival. Phase I and II clinical trials with AS101 on cancer patients showed it was non-toxic and exerted immunomodulatory effects that are associated with its beneficial clinical effects.

A number of human commercial dietary supplement products contain trace amounts of tellurium. The present invention is based on the discovery that a source of tellurium when administered orally, could positively affect the livability, weight gain or feed conversion efficiency of animals raised for meat production, and especially poultry. No one has added tellurium compounds to animal feed.

SUMMARY OF THE INVENTION

The invention comprises the administration in a pharmaceutically acceptable carrier, including animal feed, of an effective amount of a source of tellurium to improve the health and enhance the livability, cumulative weight gain and feed conversion efficiency of poultry and other animals such as cattle, sheep, goats, pigs, rabbits and the like. One or more objects of the present invention are accomplished by the provision of a method of supplementing standard feed with a source of tellurium. The tellurium may be administered as free tellurium, inorganic tellurium or organic tellurium and fed immediately after hatching or birth, or to animals afflicted with, or susceptible to, poor growth performance. Organic

tellurium is preferred.

Accordingly, it is a primary object of the present invention to provide a method to enhance growth performance and feed conversion efficiency, prevent poor growth performance in animals susceptible to same, or treat poor growth performance in animals raised for meat production, and especially poultry using a source of tellurium. The method comprises feeding the newborn animals a tellurium supplemented diet at a point in time preferably within the first five days of birth, more preferably within the first three days of birth.

It is an object of the present invention to provide a feed composition with which the undesired mortality of newborn animals, and especially young chicks can be reduced.

It is also an object of the present invention to provide a novel feed composition which is resistant to degradation, nontoxic, low cost, readily assimilable, does not leave a toxic residue in the meat of animals, can be packaged in bulk, shipped and divided into dosage unit form at the point of use. The process should be carried out efficiently and meet requirements important for commercial production.

These and other objects of the invention will become apparent from a review of the specification.

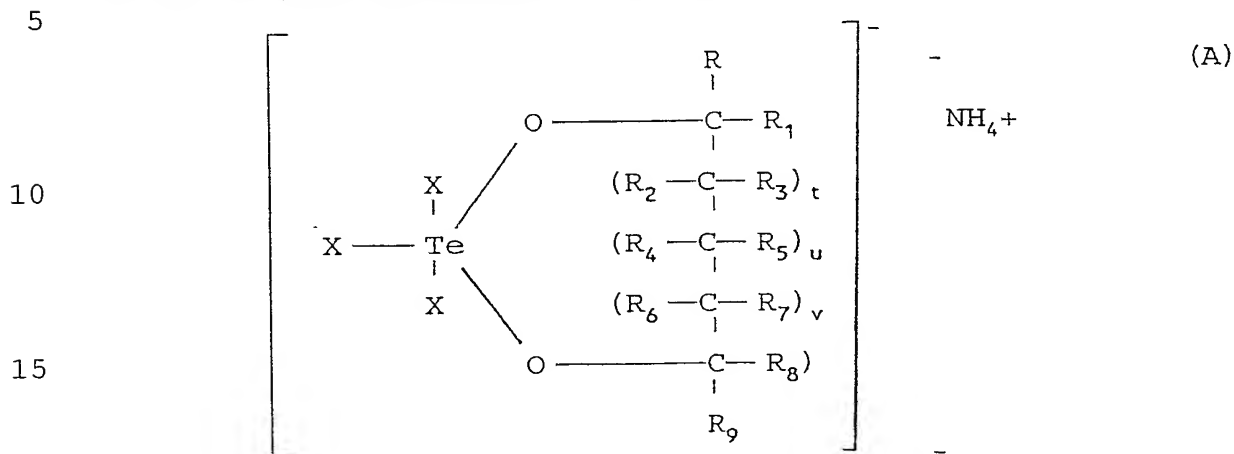
DETAILED DESCRIPTION OF THE INVENTION

Surprisingly, it has been discovered that the growth of poultry can be stimulate and the livability, cumulative weight gain and feed conversion efficiency of the poultry can be improved by feeding a formulation of the present invention.

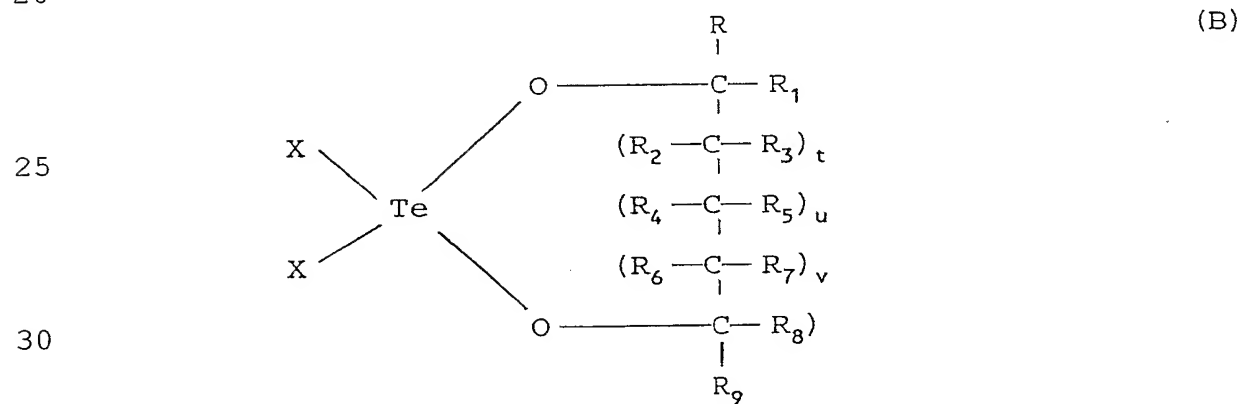
An advantage of the present invention is to increase the livability of animals raised for meat production, and especially poultry, using the feed composition of the present invention. "Livability" is judged by determining the proportion of animals on a particular feed regimen that are alive after a particular period of time. When poultry are grown for food production, there is generally a loss of a small, but constant, percentage of the animals prior to bringing the animals to market. This means that the feed eaten prior to death of the animals and the other costs expended on the animals that do not survive are wasted. The decrease in death rate of the animals during the growing period of the present invention and improved feed conversion efficiency, results in reduced costs of raising such animals.

The compositions can also be used in a feed composition as a treatment for the

The term "organic tellurium" is defined to mean any tellurium element bonded to an organic moiety, including via atoms that differ from carbon, such as oxygen. Preferred organic tellurium compounds for use in the present invention are described in 37 INORG. CHEM. 1707 (1998) incorporated herein by reference and include those of the formula:



or



or

Te(ethylene glycol)₂Te(citrate)₂

An organo or inorgano compound containing tellurium oxide

or

TeO₂ or complexes of TeO₂

(C)

or

PhTeCl₃

(D)

5

or

TeX₄, when X is Cl, Br or F

or the following complex: TeO₂.HOCH₂CH₂OH.NH₄Cl;

10

or

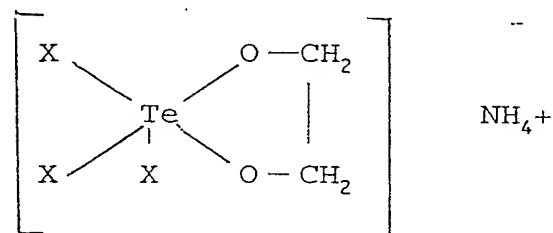
(C₆H₅)₄P⁺(TeCl₃(O₂C₂H₄))-

(E)

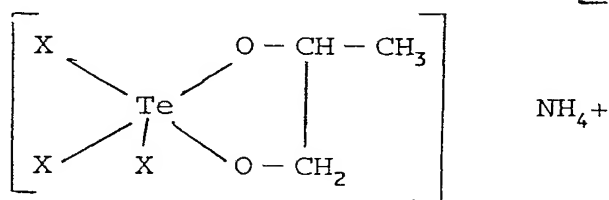
wherein t is 1 or 0; u is 1 or 0; v is 1 or 0; R, R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, and R₉ are the same or different and are independently selected from the group consisting of hydrogen, hydroxyalkyl of 1 to 5 carbons, hydroxy, alkyl or from 1 to 5 carbon atoms, halogen, haloalkyl of 1 to 5 carbon atoms, carboxy, alkylcarbonylalkyl of 2 to 10 carbons, alkanoyloxy of 1 to 5 carbon atoms, carboxyalkyl of 1 to 5 carbons atoms, acyl, amido, cyano, amidoalkyl of 1 to 5 carbons, N-monoalkylamidoalkyl of 2 to 10 carbons, N,N-dialkylamidoalkyl of 4 to 10 carbons, cyanoalkyl of 1 to 5 carbons alkoxy of 1 to 5 carbon atoms, alkoxyalkyl of 2 to 10 carbon atoms and -COR₁₀ wherein R₁₀ is alkyl of 1 to 5 carbons; and X is halogen; while the ammonium salt is illustrated, it is understood that other pharmaceutically acceptable salts such as K⁺ are within the scope of the invention. The compounds with the five membered rings are preferred.

As used herein and in the appended claims, the term alkyl of 1 to 5 carbon atoms includes straight and branched chain alkyl groups such as methyl; ethyl; n-propyl; n-butyl, and the like; the term hydroxyalkyl of 1 to 5 carbon atoms includes hydroxymethyl; hydroxyethyl; hydroxy-n-butyl; the term haloalkyl of 1 to 5 carbon atoms includes chloromethyl; 2-iodoethyl; 4-bromo-n-butyl; iodoethyl; 4-bromo-n-pentyl and the like; the term alkanoyloxy of 1 to 5 carbon atoms includes acetyl, propionyl, butanoyl and the like; the term carboxyalkyl includes carboxymethyl, carboxyethyl, ethylenecarboxy and the like; the term alkylcarbonylalkyl includes methanoylmethyl, ethanoylethyl and the like; the term amidoalkyl includes -CH₂CONH₂; -CH₂CH₂CONH₂; -CH₂CH₂CH₂CONH₂ and the like; the term cyanoalkyl includes -CH₂CN; -CH₂CH₂CN; -CH₂CH₂CH₂CN and the like; the alkoxy, of 1 to 5 carbon atoms includes methoxy, ethoxy, n-propoxy, n-pentoxy and the like; the terms halo and halogen are used to signify chloro, bromo, iodo and fluoro; the term acyl

the like; the term aryl includes phenyl, alkylphenyl and naphthyl; the term N-monoalkylamidoalkyl includes $-\text{CH}_2\text{CH}_2\text{CONHCH}_3$, $-\text{CH}_2\text{CONHCH}_2\text{CH}_3$; the term N,N-dialkylamidoalkyl includes $-\text{CH}_2\text{CON}(\text{CH}_3)_2$; $\text{CH}_2\text{CH}_2\text{CON}(\text{CH}_2\text{-CH}_3)_2$. The tellurium based compounds that are preferred include those of the formula:

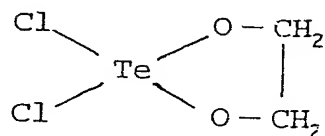


and

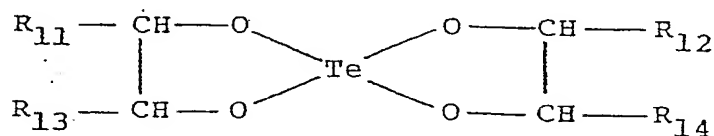


wherein X is a halogen. The preferred halogen species is chloro.

Other compounds which are based on tellurium and may be used in the practice of the invention include PhTeCl_3 , TeO_2 , $\text{TeO}_2 \cdot \text{HOCH}_2\text{CH}_2\text{OH} \cdot \text{NH}_4\text{Cl}$ and $\text{TeX}_4 (\text{C}_6\text{H}_5)_4 \text{P}^+ (\text{TeCl}_3(\text{O}_2\text{C}_2\text{H}_4))^-$ (Z. Naturforsch, 36, 307-312 (1981)). Compounds of the following structure are also included:



Other compounds useful for the practice of the present invention include:



wherein R₁₁, R₁₂, R₁₃ and R₁₄ are independently selected from the group consisting of hydrogen, hydroxy-alkyl of 1-5 carbons atoms, hydroxy and alkyl of 1-5 carbons atoms.

Useful dihydroxy compounds for use in the preparation of compounds of structure A or B, include those of formula I wherein R, R₁, R₄ and R₅ are as shown in the Table:

TABLE



R	R ₁	R ₄	R ₅
H	H	H	H
H	Cl	H	H
H	OCH ₃	H	H
H	COOCH ₃	H	H
H	H	CN	H
H	CHO	H	H
H	H	COOH	H
H	CH ₂ COOH	H	H
H	H	CH ₂ COOCH ₃	H
H	I	H	H
H	H	Br	H
H	H	CONH ₂	H
H	H	CH ₂ OH	H
H	COOH	H	H

Other dihydroxy compounds for use in the preparation of compounds A and B include those of formula II wherein R, R₁, R₂, R₃, R₄ and R₅ are as shown in the Table:

5	$ \begin{array}{c} \text{R} \quad \text{R}_2 \quad \text{R}_4 \\ \quad \quad \\ \text{HO}-\text{C}-\text{C}-\text{C}-\text{OH} \\ \quad \quad \\ \text{R}_1 \quad \text{R}_3 \quad \text{R}_5 \end{array} \quad (\text{II}) $					
10	R	R ₁	R ₂	R ₃	R ₄	R ₅
	H	H	H	H	H	H
	H	H	Cl	H	H	H
15	H	CH ₂ OH	H	H	H	H
	H	H	OH	H	H	H
	H	H	H	CH ₃	H	H
	H	H	H	CH ₂ Cl	H	H
	H	H	H	COOH	H	H
20	H	H	H	CH ₂ COOH	H	H
	H	H	H	CHO	H	H
	H	H	H	H	H	CH ₂ CHO
	H	H	CONH ₂	H	H ₂	CH ₃
	H	H	H	CN	H	H
25	H	H	H	H	CH ₂ CONH ₂	H
	H	H	H	COOCH ₃	H	H
	H	H ₃	OCH ₃	H	H	H

30

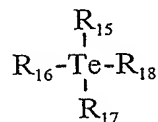
Other dihydroxy compounds for use in making compounds of formula A and B include those of formula III wherein R, R₁, R₂, R₃, R₄ and R₅ are as shown in the Table.

5	<hr/>								
	<div style="text-align: center;">$\begin{array}{ccccccc} & & R & R_2 & R_4 & R_8 & \\ & & & & & & \\ HO & -C & -C & -C & -C & -OH \\ & & & & & & \\ & & R_1 & R_3 & R_5 & R_9 & \end{array}$</div>								(III)
10	<hr/>								
	R	R ₁	R ₂	R ₃	R ₄	R ₅	R ₈	R ₉	
15	<hr/>								
	H	H	H	H	H	H	H	H	
	H	H	Cl	H	H	H	H	H	
	H	H	H	H	Br	H	H	H	
20	H	H	OCH ₃	H	H	H	H	H	
	H	H ₂	CONH ₂	H	H	H	H	H	
	H	Br	H	H	Br	H	H	H	
	H	H	H	H	CH ₂ COOH	H	H	H	
	H	H	Cl	Cl	H	H	H	H	
25	H	CH ₂ COOH	H	H	H	H	H	H	
	H	H	CH ₃	H	H	H	H	H	
	H	CH ₃	H	H	H	H	H	H	
	H	CH ₂ Cl	H	H	H	H	H	H	
	H	H	H	I	H	H	H	H	
30	H	CH ₂ CN	H	H	H	H	H	H	
	H	H	H	H	CH ₂ CH ₂ OH	H	H	H	

Additional dihydroxy compounds include those of formula IV wherein R, R₁, R₂, R₃, R₄ and R₅ are as shown in the Table.

5	<div style="text-align: center;">$\begin{array}{c} \text{R} \quad \text{R}_2 \quad \text{R}_4 \quad \text{R}_6 \quad \text{R}_8 \\ \quad \quad \quad \quad \\ \text{HO}-\text{C}-\text{C}-\text{C}-\text{C}-\text{R}-\text{OH} \\ \quad \quad \quad \quad \\ \text{R}_1 \quad \text{R}_3 \quad \text{R}_5 \quad \text{R}_7 \quad \text{R}_9 \end{array}$</div>										(IV)
10	R	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈	R ₉	
<hr/>											
15	H	H	H	H	H	H	H	H	H	H	
	H	H	Cl	H	H	H	Cl	H	H	H	
	H	H	Cl	Cl	H	H	H	H	H	H	
	H	H	CONCH ₃	H	H	H	Br	H	H	H	
	H	H	Br	H	H	H	CON(CH ₃) ₂	H	H	H	
20	H	H	H	OCH ₃	H	H	H	H	H	H	
	H	H	H	H	OCH ₃	H	H	H	H	H	
	H	H	H	H	CH ₂ COOH	H	H	H	H	H	
	H	H	COOH	H	H	H	H	H	H	H	
	H	CH ₃	H	H	H	H	H	H	H	H	
25	CH ₃	H	H	H	H	CH ₃	H	H	H	H	
	H	CH ₂ CH ₃	H	H	H	H	H	Cl	H	H	
	H	CH ₂ CN	H	H	CH ₂ OH	H	H	H	H	H	
	H	H	H	I	H	H	H	H	CN	H	
	H	CH ₂ CH ₂ COOH	H	H	H	H	H	H	H	H	
30	H	H	CHO	H	H	H	H	H	H	H	
	H	H	H	F	H	H	H	H	H	H	

Compounds of the following formula are also included:



herein R_{15} , R_{16} , R_{17} and R_{18} are independently selected from halogen, alkyl of 1-5 carbons; aryl, acyl of 1-5 carbon hydroxyalkyl of 1-5 carbons and aminoalkyl of 1-5 carbons may be made by reacting the appropriate di, tri or tetrahalotelluride with the appropriate hydroxy compound which may be of the formula: $HO-R_{19}$;

wherein R_{19} is an alkyl of 1 to 5 carbons, haloalkyl of 1 to 5 carbons, aryl, alkylaryl, alkylamido of 1 to 5 carbons, alkylcarbonyl of 1 to 5 carbons, cyanoalkyl of 1 to 5 carbons, cyanoalkyl of 1 to 5 carbons, and an alkoxyalkyl of 2 to 10 carbons. Specific examples of R_{16} include methyl, ethyl, n-propyl, phenyl, tolyl, amidoethyl, cyanomethyl, methyloxymethyl and CH_2CH_2COOH .

These compounds are described in U.S. 4,761,490, which is incorporated by reference herein. In addition, inorganic tellurium compounds such as $TeCl_4$, $TeBr_4$ and compounds which give TeO_2 in aqueous solution, preferably in the form of a complex, such as a TeO_2 complex with citric acid or ethylene glycol may be used.

The preferred compound is ammonium trichloro (dioxoethylene-O,O') tellurate. The tellurium compound may be administered orally, via yolk sac injection, parenterally, in ovo, or via inhalation by spray. The parenteral route of administration may be intravenously, subcutaneously, intramuscularly, etc. The composition of the present invention will mostly be supplied in the solid state, for example as a powder, in pellets or crumbs.

In one embodiment of the present invention, the source of tellurium may be administered orally, added to the standard feed and direct fed or administered via a compatible liquid vehicle. It may be supplied as such or mixed with conventional nutrients such as, for example corn or soya. It will be understood by those skilled in the art that the active tellurium derivatives described herein can also be fed in combination with together commercially formulated or similar feeds for chickens and other animals. Tellurium is preferably combined with the feed by mixing to evenly distribute. Adding a fixed amount of tellurium directly to the feed has the advantage of convenience and is more economical than weighing animals and adjusting dosages each day.

The dosage of ammonium trichloro (dioxoethylene-O,O') tellurate, a pharmaceutically acceptable salt thereof, or other selenium or tellurium compound varies depending on the administration route, ages, weights and animal type. It may be in the range

from 0.1 gram to 20 grams per metric ton of feed, preferably from 0.2 to 1.0 gram per metric ton, most preferably 0.5 grams per metric ton, and especially 0.5 grams per metric ton for poultry, administered daily in one or more divided doses, preferably with food. If desired, the selenium or tellurium compound may be administered in drinking water that is provided to animals.

It has been found that the tellurium compounds useful in the practice of the present invention will hydrolyze in the presence of water. These hydrolyzed compositions are active in vivo and in vitro although the hydrolyzed compositions eventually decompose and lose their ability to induce lymphokine secretion. For this reason, the compositions should be freshly prepared. Preferably, the compounds should be kept under anhydrous conditions until just prior to being used.

The tellurium may also be administered with vitamin, microbial (e.g. Lactobacillus), antimicrobial, enzyme, and forage additives. Examples of antibiotics approved for use in animal feed include bacitracin, bacitracin methylenedisalicylate, lincomycin, or virginiamycin. Vitamin additives may be selected from vitamins A, B1, B6, B12, biotin, choline, folic acid, niacin, panthothenic acid, riboflavin, C, D, E, and K. Mineral additives may be added from calcium, phosphorous, selenium, chlorine, magnesium, potassium, sodium, copper, iodine, iron, manganese, chromium, and zinc. The concentration of the vitamins and minerals will generally be between about 0.01% and about 5% by weight of the dry matter.

In another embodiment of the present invention, the source of tellurium may be combined with immunoactive agents, such as vaccines; other therapeutic drugs, such as growth promoters or hormones; digestion enhancers, such as bile salts; palatability modifiers, such as spices or gums; or feed intake regulators, such as food coloring.

A variety of other substances can be employed as adjuvants in the present invention. Some examples include: polysaccharides, peptides, macromolecules.

The ratio of selenium to tellurium in the feed composition can be in the range between about 1:1 and about 1:50.

In addition to chickens, the nutritional composition is equally effective in enhancing growth in other animals including turkeys, pheasants, ducks, cattle, sheep, goats, pigs, rabbits and the like.

The nutritional food requirements of the above listed animals are known to those skilled in the art. The present invention is administered to said animals by the addition of selenium and tellurium to said nutritional food requirements.

EXAMPLE 1

5 The dosage of ammonium trichloro (dioxoethylene-O,O') tellurate, or a pharmaceutically acceptable salt thereof, varies depending on the administration route, age, weight and type of animal. In addition, it may be in the range from 0.1 gram to 20 grams per metric ton, preferably from 0.2 to 1.0 gram/ metric ton, and most preferably 0.5 grams per metric ton, administered daily in one or more divided doses, preferably with food.

10 The efficiency of the invention has been demonstrated in three-day-old inanited chicks where three concentrations of AS101 were introduced into the feed (500-12,500 mg/metric ton) for three weeks. Each chick included in the study weighed exactly 80 g. via accurate electronic scale. Also, each chick was marked. There were five different treatment groups, each group comprising ten chicks in four repetitions. The five groups of animals
15 were tested as follows: Group 1 received a standard feeding diet without selenium; Group 2 received the standard feeding diet supplemented with 300 mg/metric ton of selenium; Group 3 received the same diet as Group 2 with the addition of AS101 at a concentration of 500 mg/metric ton; Group 4 received the same diet as Group 2 with the addition of AS101 at a concentration of 2,500 mg/metric ton; Group 5 received the same diet as Group 2 with the
20 addition of AS101 at a concentration of 12,500 mg/ton. All the experiments were randomized and open. The results of each group represent the mean of 40 chicks.

For growth period days 3-24, the performance of groups of three day old birds, fed AS101 concentrations of 500 mg/metric ton, 2,500 mg/metric ton or 12,500 mg/metric ton were compared to groups of control birds fed either a standard feeding diet without selenium
25 or a standard feeding diet with an addition of 300 mg/metric ton selenium. Body weight (BW) was measured after 24 days. At the end of 24 days, the animals were examined for gross signs of toxicity. A gross visual examination was carried out. The liver of each chick was extracted and weighed. No pathological changes were observed in histological studies. The survival rate was 100%. Since there were no mortalities in any group, it is clear that
30 AS101 had an effect on livability.

Results are presented in Table 1. The group with the lowest mean body weight was Group 1, where the diet was the standard feeding diet without selenium. Group 2, which was fed the diet of Group 1, with an addition of 300 mg/ton of selenium showed a 6.0% increase in BW over Group 1. The increase in BW is caused by the addition of the selenium to the
35 mixture.

Addition of AS101 to the same diet as Group 2 resulted in the highest feed efficiency. The addition of AS101 to the mixture, that includes selenium, showed a BW increase of 1.7% at a concentration of 500 mg/ton, 2.3% at a concentration of 2,500 mg/ton, and 5% at a concentration of 12,500 mg/ton. Group 5, which was fed the highest level of tellurium, showed a 5.4% increase in BW over Group 2.

It appears that food intake is not altered by feeding with AS101. At day 21 the difference is only 12 g or about 1%. The differences in BW between AS101 supplemented and unsupplemented groups was highly significant, even though feed intake was almost identical in all groups.

DATA TABLE 1

PERFORMANCE DATA OF CHICKS AT THE GROWTH PERIOD 3-21 DAYS DIET WITH AS101

TREAT- MENT #	BW-24D (g.)	BW, % OF CONTROL (%)	FEED INTAKE (g.)	FEED EFFICIENCY (g./g.)	FE, % OF CONTROL (%)	LIVER, % OF BW (%)
1	1013	94.6	1376	0.679	96.2	2.36
2	1072	100	1405	0.706	100	2.32
3	1090	101.7	1382	0.731	103.5	2.36
4	1097	102.3	1375	0.74	104.8	2.48
5	1126	105	1417	0.738	104.5	2.39

These results reconfirm the essential nature of selenium in the poultry diet, and the experiment facility's sensitivity in detecting the tellurium benefits to the growth, gain and feed efficiency of 24 day old chicks.

The foregoing description of the invention has been presented for purposes of illustration

and description. It is not intended to be exhaustive or to limit the invention to the precise form disclosed. Obvious modifications or variations are possible in light of the above teachings. All such obvious modifications and variations are intended to be within the scope and spirit of the appended claims.

EXAMPLE 2

Two hundred and eighty 3 day-old White Rock broiler chicks were distributed into 28 replicate-groups, 4 groups for each one of the 7 treatments. They were reared in electrically heated battery brooders till an age of 24 days, and afterwards were transferred to individual cages in a room at 22°C. Light was provided constantly. Individual body weights, mortality and feed consumption on a group basis were recorded weekly.

The treatments were as follows:

1. Negative control, standard chicks diet with no supplements;
2. Same as 1 with addition of 300 mg AS101 per ton of feed;
3. Same as 1 with addition of 1000 mg AS101 per ton of feed;
4. Same as 1 with addition of 3,000 mg of AS101 per ton of feed;
5. Same as 1 with addition of 1,500 mg of TeO₂ per ton of feed;
6. Same as 1 with addition of 4,500 mg of TeO₂ per ton of feed;
7. Same as 1 with addition of 13,500 mg of TeO₂ per ton of feed.

The composition of the experimental diet is shown in Data Table 2. The diet was formulated to meet NRC requirements for broiler chicks that were fed *ad libitum* in mash form. Water was supplied *ad libitum*.

DATA TABLE 2.

Composition of broiler diets (kg/ton).

INGREDIENTS		AGE PERIODS
		24-45 day
	Corn	500
10	Sorghum	84
	Soybean meal	324.7
	Fish meal	-
	Soybean oil	55
	Limestone	10
15	Dicalcium phosphate	20
	Table salt	2.5
	DL-Methionine	1
	Vitamin premix ¹	2.5
	Mineral mix ²	0.3
20	<u>Calculated Analyses:</u>	
	Metabolizable energy (kcal/kg)	3190
	Crude protein, %	19.5
	SAA, %	0.73
25	Lysine, %	1.09
	Calcium, %	0.94
	Phosphorus (Av), %	0.46

¹The Vitamin premix supplied (per metric ton of diet): retinol, 2.52 mg; cholecalciferol, 50 µg; tocopherol acetate, 24 mg; menadione sodium bisulphite, 2 mg; thiamine 1.5 mg; riboflavin 5.6 mg; calcium pantothenate 15 mg; niacin 50 mg; pyridoxine 5 mg; folic acid 2 mg; cyanocobalamin 15 µg. choline chloride 300 mg and Ethoxyquin 125 mg.

²The minerals mix supplied (per metric ton of diet): Mn, 80 mg; Zn, 50 mg; Cu, 5 mg; Mo, 1.6 mg; Co, 300 µg; I, 1.2 mg; Fe, 20 mg; Se, 300 mg.

Means were subjected to analysis of variance (Snedecor and Cochran, 1967) and to a multiple range test.

The study was developed to investigate the effects of AS101 and TeO₂ supplements on the performance of broiler chicks. For this purpose NRC broiler diets were used which differ
5 only in the new supplements.

Data Table 3 shows significant improvement in weight gain compared to the control data (i.e. without supplements) by 4.2-5.8%. The improvement in feed efficiency, by 4.8-7.1%, was statistically significant compared with the control data.

Data regarding the broilers' body composition at the age of 45 days (Data Table 4)
10 indicates that the addition of AS101 and TeO₂ to their diet improved the amount of whole carcass by 0.9-1.7% (not always significantly), compared to the control data. No differences in carcass size were found with treatments of AS101 and TeO₂ supplements. In addition, the effect of AS101 and TeO₂ upon other parts of broilers' body was also not found.

The birds in the experiment did not show any disorders, which could be explained by the
15 use of AS101 and TeO₂ supplements in their diets.

The examination of AS101 and TeO₂ in the broilers at the age period of 3-45 days shows that the highest positive effect on birds performance occurs at the dosage of 3,000 mg/ton of feed for AS101 and at all dosages for TeO₂.

20

25

DATA TABLE 3

Performance of broiler chicks fed diets with AS101 and TeO₂ supplements (*whole raising period*)¹

		T r e a t m e n t s						
		1	2	3	4	5	6	7
<u>Age period 3-45 days</u>								
	Body weight 45 d, g	2537b	2641a	2652a	2680a	2675a	2666a	2663a
	<i>St. Deviation</i>	73.9	26.1	42.1	19	85.1	27.1	32.1
	Variation of BW, %	2.90	0.99	1.59	0.71	3.18	1.02	1.21
15	Weight gain, g	2465b	2569a	2580a	2608a	2603a	2594a	2590a
	<i>St. Deviation</i>	73.9	26.1	42.1	19.0	85.1	27.1	32.1
	Weight gain, % Contr.	100	104.2	104.7	105.8	105.6	105.2	105
	Feed intake, g		4351a	4256a	4245a	4349a	4296a	4371a
	<i>St. Deviation</i>		109	42.4	76.2	126.4	188.3	56.5
20	Feed intake, % Contr.	100	97.8	97.8	99.9	98.7	100.4	99.4
	Feed efficiency, g/g	0.566b	0.604a	0.608a	0.600a	0.606a	0.593a	0.599a
	<i>St. Deviation</i>		0.009	0.001	0.021	0.016	0.021	0.003
	Feed efficiency, % Cont.	100	106.7	107.4	106.0	107.1	104.8	105.8

¹ Means without a common letter differ significantly (P<0.05).

DATA TABLE 4

Body composition of 45-day old broilers fed diets with different
amounts of AS101 and TeO₂ supplements ¹

		T r e a t m e n t s						
		1	2	3	4	5	6	7
10	Carcass, % of BW	67.9b	68.7ab	69.5ab	69.6a	69.2ab	69.6a	69.5ab
	<i>St. Deviation</i>	2.5	3.1	1.15	1.66	1.23	1.65	1.17
	Breast, % of BW	16.4ab	16.5ab	16.3b	17.1a	16.7ab	16.7ab	16.8ab
	<i>St. Deviation</i>	1.52	0.68	0.64	1.11	0.62	0.94	0.69
	Abd. Fat, % of BW	1.33a	1.41a	1.54a	1.40a	1.45a	1.55a	1.41a
15	<i>St. Deviation</i>	0.32	0.28	0.43	0.44	0.27	0.32	0.45
	Heart, % of BW	0.44ab	0.44ab	0.41b	0.45ab	0.45ab	0.46a	0.44ab
	<i>St. Deviation</i>	0.047	0.056	0.035	0.045	0.050	0.046	0.101
	Liver, % of BW	1.47a	1.54a	1.55a	1.49a	1.46a	1.54a	1.43a
	<i>St. Deviation</i>	0.244	0.248	0.257	0.166	0.169	0.159	0.300

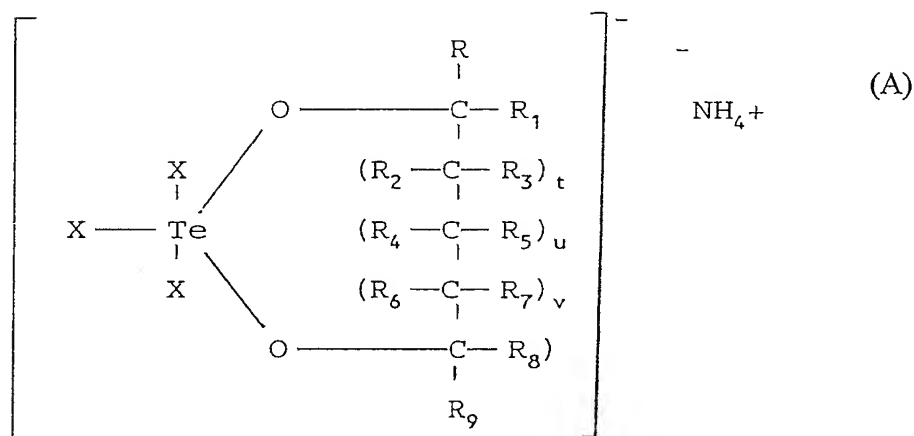
¹ Means without a common letter differ significantly (P<0.05).

CLAIMS

1. A feed composition for enhancing the weight gain or feed conversion efficiency in animals raised for meat production which comprises an effective amount of a source of tellurium.

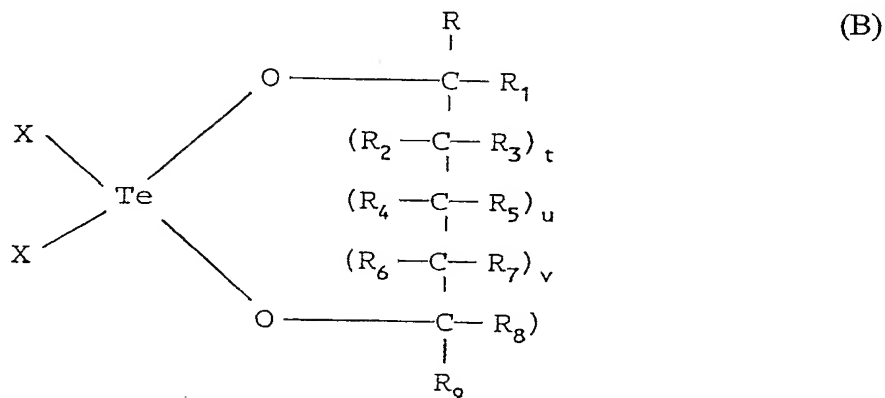
2. A feed composition as in Claim 1, wherein the source of tellurium is an organic tellurium.

3. A feed composition for enhancing the weight gain or feed conversion efficiency in animals raised for meat production, comprising an effective amount of a compound of the formula:



or the complex of $\text{TeO}_2 \cdot \text{HOCH}_2\text{CH}_2 \cdot \text{NH}_4\text{Cl}$;

or



or

TeO₂ or complexes of TeO₂ (C)

5 or

PhTeCl₃ (D)

or

(C₆H₅)₄P+(TeCl₃(O₂C₂H₄))-

or

10 TeX₄,

wherein t is 1 or 0; u is 1 or 0; v is 1 or 0; R, R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, and R₉ are the same or different and are independently selected from the group consisting of hydrogen, hydroxyalkyl of 1 to 5 carbons, hydroxy, alkyl of 1 to 5 carbon atoms, halogen, haloalkyl of 1 to 5 carbon atoms, carboxy, alkylcarbonylalkyl of 2 to 10 carbons, alkanoyloxy of 1 to 5 carbon atoms, carboxyalkyl of 1 to 5 carbons atoms, acyl, amido, cyano, amidoalkyl of 1 to 5 carbons, N-monoalkylamidoalkyl of 2 to 10 carbons, N,N-dialkylamidoalkyl of 4 to 10 carbons, cyanoalkyl of 1 to 5 carbons alkoxy of 1 to 5 carbon atoms, alkoxyalkyl of 2 to 10 carbon atoms and -COR₁₀ wherein R₁₀ is alkyl of from 1 to 5 carbons; and X is halogen and complexes thereof.

20

4. A feed composition as defined in Claim 3 wherein the compound is a tellurium compound which is ammonium trichloro (dioxoethylene-O,O') tellurate or the complex of TeO₂, ethylene glycol and ammonium chloride.

25

5. A feed composition as defined in Claim 3 wherein the source for tellurium is TeO₂.

6. A method, according to Claim 1, for enhancing weight gain in poultry.

30

7. A method for enhancing weight gain in poultry, comprising orally administering to said poultry a feed composition comprising, as an active ingredient, tellurium compounds as defined in Claim 3.

8. A method for enhancing the weight gain in poultry by feeding a feed composition comprising, by weight of the diet,

35

(a) a standard feeding diet containing about 0.2 ppm of a non-toxic source of selenium; and

(b) about 0.2 ppm of a tellurium compound.

5 9. A dietary supplement for enhancing weight gain in poultry comprising

(a) a non-toxic source of selenium; and

(b) a tellurium compound.

10 10. A dietary supplement for enhancing weight gain in poultry, as set forth in claim 9, wherein the tellurium compound is organic tellurium.

11. A feed composition, as defined in Claim 3, wherein the tellurium compound is administered in combination with at least one vitamin or trace element.

15 12. A feed composition, as defined in Claim 3, wherein the tellurium compound is administered in combination with at least one medicament ingredient from the group consisting of antibiotics, vaccines and growth enhancers.

20 13. A feed composition, as defined in Claim 3, wherein the tellurium compound is administered in combination with trace elements either singly or in combination which includes cobalt, copper, manganese, iron, zinc, tin, nickel, chromium, molybdenum, iodine, chlorine, silicon, vanadium, selenium, calcium, magnesium, sodium and potassium.

25 14. A composition, as defined in Claim 3, wherein the tellurium compound is administered in combination with selenium.

15. A composition, as defined in Claim 3, wherein the non-toxic selenium source is sodium selenite.

30 16. A composition, as defined in Claim 3, wherein the tellurium compound is administered orally.

35 17. A composition, as defined in Claim 1, wherein the compound is administered in combination with vitamins either singly or in combination chosen from the group consisting of thiamine HCl, riboflavin, pyridoxine, niacin, inositol, choline chloride, calcium

pantothenate, biotin, folic acid, ascorbic acid, vitamin B12, p-aminobenzoic acid, vitamin A, vitamin K, vitamin D, vitamin E.

5 18. A pharmaceutical composition which comprises a therapeutically effective amount of the compound as set forth in Claim 3 in admixture with a pharmaceutically acceptable carrier or diluent.

10 19. A method of feeding for enhancing growth of poultry, prophylaxis or treatment, which comprises administering to said poultry a therapeutically effective amount of the compound as set forth in Claim 3.

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(54) Title: TELLURIUM CONTAINING PRODUCT

(57) Abstract: A novel nutrient formulation containing tellurium for use in animals raised for meat production, and a method of feeding said nutrient formulation which improves subsequent livability, cumulative feed efficiency or weight gain is disclosed.



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Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- A	US 4,929,739 A (SREDNI et al) 29 May, 1990 (29.05.1990), see entire document.	1-3, 18 ----- 4-17, 19
A	US 4,946,437 A (SREDNI et al) 07 August 1990 (07.08.1990), see entire document.	1-19
A	US 5,093,135 A (ALBECK et al) 03 May 1992 (03.05.1992), see entire document.	1-19



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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